obligation to the people of this State to preserve the high standards of medical care and to make that care available on an economic basis within the reach of the vast majority of the people. If we do this, and only if we do it, can we be reasonably secure.

As citizens we have a serious duty to aid in barring the advance of socialism. Medicine in this country has already come under attack. It has been chosen as the first victim by the planners but it is apparent that they intend to include all forms of endeavor within their scope. If one element of private enterprise falls, a breach has been made in the defenses of all and the authoritarian state is that much nearer its objectives.

I am convinced of the truth of the statement of Frederick Hayek in his book "The Road to Serfdom" when he says: "The slave state always starts out as a 'welfare state'. It promises freedom from want, worry—as many freedoms as you wish, except freedom from the state itself!"

If we do not exert every effort to prevent this from transpiring we are defaulting in our obligation as physicians and citizens. The greatest weakness we could have would be division among us. This is no time for dissension, petty quarrels or selfishness.

I therefore urge upon you the importance of the unity of the profession, of supporting and furthering the program of your Association and of standing firm against the forces which would subject you and the public to regimentation with serious injury to both.

A unified profession determined to resist socialization cannot be enslaved. But in the words of Abraham Lincoln, "A house divided against itself cannot stand."

Hypersensitivity, the Common Denominator of the Collagenous Diseases

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RECENT advances in the treatment of the simple allergies plus the revival of interest in rheumatic fever calls attention to a group of related diseases, cousins, one might say, of the common allergic entities.

Rheumatic fever, periarteritis nodosa, disseminated lupus erythematosis, dermatomyositis, serum sickness, various drug allergies, and possibly regional enteritis are all well known clinical entities. The variations in the individual clinical and general pathological patterns permit differentiation of a goodly number of these diseases. There remain, however, those intermediate cases which the pathologist is hard put to file into a diagnostic pigeon hole. They possess in common one fundamental histopathological lesion, degenerative and fibrinoid alteration of collagen, the intercellular substance which lends strength to connective tissue and forms an important constituent of blood vessel walls. Vascular lesions play the leading role in the pathological features of this group so the term "visceral angiitis" has been used. The different organ distribution of the vascular lesions, the relative degree of involvement of the serosal and endocardial surfaces and the interstitial tissue, the degree of collagenous changes, and the cellular response of the organism set the pattern for that particular disease.

Banks [2] pointed out the striking similarity in the microscopic lesions of disseminated lupus erythematosis, dermatomyositis, scleroderma, and periarteritis nodosa. The differentiation among them is dependent upon the dominant individual focal lesions, age, sex predilection, and the course of the disease. Fox [6] feels that disseminated lupus erythematosis is an allergic disease while Rich in numerous publications points out the allergic basis for rheumatic fever and periarteritis as well as serum sickness.

Let us examine the evidence for a common mechanism of evolution for the entire group, namely: antigen-antibody reaction in the tissue cells of a hypersensitive organism.

Anaphylaxis, the Arthus phenomenon, and serum sickness are different patterns of the allergic state. The type of reaction will depend upon the antigen, the dose, frequency of the dosage, the route of entry, and the individual sensitivity. The individual sensitive to horse serum will react to intracutaneous administration of the serum with a violent wheal while if enough serum were to be given intravenously, he would likely die in anaphylaxis. The hypersensitive state is not a protective mechanism related to immunity.

The injection of a heterologous serum, horse antitetanus serum for example, into a human stimulates the formation of antibodies against fractions of the horse serum, probably the globulin. If the rise in anti-horse antibodies is rapid enough, a significant titre will be reached before the horse antigens have disappeared. The reaction of antigen with antibody produces serum sickness, the individual symptoms depending upon which group of body cells the antibodies have become fixed.

Clark and Kaplan [3] report two deaths following large doses of anti-pneumococcus serum. Pathologically there was proliferation of histiocytes in the valvular and mural endocardium, the intima of the aorta and pulmonary artery, and the interstitial tissue of the heart, liver, kidneys, and adrenals. Collagen fragmentation and periarterial cellular proliferation were seen in the more severe lesions.

Similar collagenous lesions were seen in the two children reported by Werne and Garrow [23] who died in anaphylaxis following a second dose of diphtheria toxoid.

The rabbit equivalent of serum sickness may be produced by a single large dose of heterologous serum. The rabbits become ill, febrile, and there is flushing of the ears.

In the study of living vessels in the rabbit ear, Abel and Sheck [1] found arteriolar constriction and migration of leukocytes through the capillary walls. Repeated doses of antigen produced focal endothelial destruction.

Rich [17] reports seven fatal pneumonia cases, in five of which the patient received both serum and a sulfonamide; in one, serum alone; and in one a sulfonamide alone. Six had symptoms of serum sickness before death. In each of these patients there was found at postmortem the typical early lesions of periarteritis nodosa, namely: necrosis, fibrinoid, and hyalin alteration of the collagen in the media of arteries, mononuclear and polymorphonuclear infiltration of the vessel walls and perivascular areas, and in four cases infiltration with eosinophils. Rich later reported another case [18] in which a skin biopsy before sulfonamide therapy demonstrated normal vessels but the postmortem examination revealed typical vascular lesions. Comparable lesions following sulfonamides have been reported by Merkel and Crawford [13] and Lederer and Rosenblatt.[10] The similarity of rheumatic pneumonitis and the allergic pneumonitis due to the sulfonamides has been pointed out by Rich and Gregory.[19]

According to McCall,[12] in periarteritis nodosa the fibrinoid degeneration of the media and the subendothelial cellular proliferation may involve any or all grades of blood vessels. Later manifestations are periarterial granulomas and aneurysms. All organs may be involved. The classical case with abdominal, pulmonary, cardiac, renal, muscular, and skin symptoms and signs offers little diagnostic difficulty.

Bronchial asthma is a typical allergic disease. It may run a fairly benign course for decades, yet the asthmatic always treads a perilous path. Rackemann [15] stresses the relationship of asthma to periarteritis and points out the unfavorable prognostic sign of a rising eosinophile count, especially if associated with multiple areas of pneumonitis. These signs may anticipate a full-blown periarteritis nodosa. The Loeffler syndrome is therefore not always benign.

Harkavy [8] presents the records of four autopsied cases of asthma in which were present not only the typical bronchial lesions but also lesions of the blood vessels, myocardium, serous membranes, joints, skin, nervous, and hematopoietic systems. The pulmonary arterial tree showed a hyperergic reaction varying in severity from mere thickening of the media to an acute necrotizing arteritis. Similar vascular lesions were present in the heart, intestines, and other organs. The serous membrane involvement was thought to be secondary to the vascular lesions. The postmortem findings in these cases are typical of periarteritis nodosa and represent varying degrees of the allergic vascular reaction to polyvalent antigenic sensitivity.

Rich and Gregory,[20] in a brilliant series of experiments, sensitized rabbits to horse serum and then gave them repeated sublethal shocking doses. Typical lesions of periarteritis nodosa in all stages were produced: (1) edema of the endothelium and media, (2) necrosis, fibrinoid alteration, and hyalinization of the collagen of the media, and (3) marked perivascular infiltration. Diffuse glomerulonephritis was also present in some of the animals. The lesions could also be produced by a single large dose of serum. Rich's work lends additional evidence of the close relationship of serum sickness, bronchial asthma, and periarteritis nodosa.

Rheumatic fever probably causes more disability in the child and young adult than any other disease. It is of far greater importance than poliomyelitis as the cardiac cripple is more common and more handicapped than the muscular cripple. A comparison of the amount of money available for the study of these two diseases indicates a great popular lack of understanding of the facts involved.

Rantz [16] recapitulates the evidence implicating the beta hemolytic streptococcus or its products as the responsible antigen: (1) absence of rheumatic fever in the very young, (2) concomitant rise in incidence of rheumatic fever and streptococcus infections, (3) the appearance or exacerbation of the disease following a streptococcus infection, (4) high titre of anti-streptococcus lysin in the disease, and (5) cutaneous sensitivity to the streptococcus. Much credit is due Swift [22] who 16 years ago came to a similar conclusion.

Rich and Gregory [21] review the cardiac lesions generally accepted as characteristic, namely: (1) focal alteration of the collagen, (2) the Aschoff body, (3) focal and diffuse cellular infiltrations, (4) focal alterations in the cardiac muscle, and (5) valvular verrucae. The valvulitis, polyserositis, arthritis, pneumonitis, peritonitis, and erythema nodosum and marginatum are organ manifestations of the vasculitis. The authors were able to duplicate in rabbits sensitized to horse serum all these lesions, even to the Aschoff nodule, hithertofore considered to be pathognomonic of rheumatic fever.

Hall of the University of Southern California School of Medicine had produced comparable results with rabbits. No report of this work has been published. Recently Moore [14] of the same school has produced similar lesions in white mice, but using egg albumin as the antigen. Minor focal perivascular lesions have been found in the control group. This finding is of great importance, suggesting that the mouse and probably man is subjected to a host of antigens from the time he leaves the womb until he retires to the tomb. These leave their mark but the reaction is usually so slight as to cause no symptoms.

The vascular lesions of rheumatic fever and periarteritis nodosa differ in degree and distribution. In the rabbit both lesions are present.

A consideration of disseminated lupus erythema-

tosis recalls the report by Libman and Sacks [11] in 1924 in which they described what they thought to be a new clinical entity in four cases of verrucous endocarditis which was neither bacterial nor rheumatic. In retrospect, these four cases are really disseminated lupus erythematosis, an entity which had previously been described.

Coburn and Moore [4] in a study of 30 cases decide it to be predominantly a disease of young females with an onset in summer and early fall and fatal within three to eighteen months. Clinically, one sees polyserositis, arthritis, pneumonitis, renal disease, lymphadenopathy, splenomegaly, and skin lesions. If one finds the characteristic skin lesions with associated white centered petechiae, and finger tip hemorrhagic lesions, the diagnosis is simple. Many cases, on the other hand, cannot be differentiated from rheumatic fever or periarteritis nodosa.

Gross [7] and later Klemperer [9] have written detailed descriptions of the pathologic changes. The lesions resemble those of rheumatic fever and periarteritis nodosa with minor variation. Generally the collagen alteration is more marked but the cellular infiltration and reparative processes less marked than in rheumatic fever. The involvement of the interstitial tissue is more marked than in periarteritis nodosa. The most characteristic lesion, if present, is the "wire-looping" in the kidneys produced by the deposition of an unknown substance between the glomerular epithelium and capillary. Chemically, one finds an increase in the gamma globulin, that fraction of the plasma protein which is said to contain the antibodies.

These people are unusually photosensitive and acute exacerbations following sunburn have been recorded. It is thus linked to acute porphyria. Fox [6] reports a case of serum sickness which merged into disseminated lupus erythematosis.

Dermatomyositis is similar except that the course is longer and the somatic rather than the splanchnic structures are apt to be involved.

Lesions in the bowel similar to regional enteritis have been reported in periarteritis nodosa and in experimental animals shocked by foreign proteins.

SUMMARY

The diseases discussed have as the fundamental lesion collagen alteration. They are as truly manifestations of the allergic state as is asthma. The human is increasingly exposed to a host of potential antigens as soon as he is born, yet only a few develop sensitivity that results in allergic disease. Probably the single most important factor in predisposing to the allergic state is the inherent constitution of the individual. The allergy is single at first but becomes polyvalent with the passage of time.

The physician must bear in mind that many drugs, sera, and vaccines are potential antigens. Sensitization to the sulfonamides is common knowledge. One should remember that about 5 per cent of patients will have allergic reactions to penicillin, some of grave severity. Penicillin inhalations in asthmatics may make the disease more severe by adding another antigen. Penicillin in oil and wax appears to produce a higher percentage of allergic reactions than penicillin in saline.

Heterologous serum is always potentially dangerous and should be used only on definite indication. Cold vaccines in the hypersensitive individual may give trouble. Influenza vaccine contains minute traces of egg antigen and will produce severe reactions in individuals sensitive to egg. Probably it should be used only when an epidemic threatens.

Enthusiasm for massive salicylate therapy in acute rheumatic fever has waxed and waned. Coburn [5] revived interest in it in 1943. His belief that salicylates will prevent cardiac complications and reduce the occurrence of the polycyclic form is not generally shared.

The antihistamine drugs are generally effective in serum sickness and may have some promise in the other diseases.

Desensitization is rarely effective, as the sensitivity is usually polyvalent.

CONCLUSION

1. Serum sickness, periarteritis nodosa, rheumatic fever, disseminated lupus erythematosis, dermatomyositis, and perhaps regional enteritis have the common denominator of sensitivity.

2. Human lesions of collagen necrosis, fibrinoid alteration, and hyalinization, the fundamental pathological lesion in these diseases may be reproduced in animals.

3. Present therapy is not effective once angiitis is established.

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The Early Diagnosis and Radical Treatment of Prostatic Carcinoma

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INTRODUCTION

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Of all malignancies in men of all ages, cancer of the prostate is seventh in frequency, cancer of the stomach being first. But in men over 50 it is first, and with the rising expectancy of life span, it presents a problem of increasing magnitude.

Cancer is a leading cause of death in this country, and the only certain cure has been early diagnosis and radical removal. This principle, universal for other cancers such as of the breast, the stomach and the rectum, has been restricted in its application to the cure of cancer of the prostate. The reasons for this may be the uncertainty and rarity of early diagnosis, the suspected formidability of radical operation and the recent palliative promise of estrogens. The urologic staff of the University of California has practiced the radical principle of treatment for over 30 years now. The author of the following paper has reviewed the records of both private and clinic patients of all members of resident and attending staffs of this period from four different hospitals, and the analysis he gives is based on these records uninfluenced by memory or impression. The points at issue: How many patients will be cured by early diagnosis and radical surgery? What are the risks at operation and afterward? Does this surgical principle (widely applied elsewhere) apply to cancer of the prostate?

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Read before the section on Urology at the Annual Session of the California Medical Association, April 30-May 3, 1947, Los Angeles.

THERE are still urologists who find no place for radical prostatectomy in the treatment of prostatic carcinoma, saying that it is incurable if it has reached a stage at which it can be suspected before operation and that consequently the only way to treat it is by palliation with resection and hormones. The confounding thing in their point of view is that they are 95 per cent right, for even today about 95 per cent of all cases of prostatic cancer are seen when the cells have spread beyond the capsule and so cannot be excised with hope of cure. We can show, however, in our analysis of early cases that the remaining 5 per cent should not be set aside as hopeless but should be treated by radical surgical operation with a good chance for cure.

We have analyzed all the cases diagnosed as "early" by rectal palpation by the staff of the Division of Urology, University of California, in the last 20 years. The total is 45 cases. In eight of these cases the cancer was found to have spread beyond the capsule at operation. However, these cases are included in the analysis. Three other cases were not included because of inadequate operative or follow-up information. For comparison, we have reviewed recently published reports of series of unmetastasized carcinoma.

Prostatic carcinoma differs from cancer of most other organs in two important ways. It originates in a part of the body fairly inaccessible to usual radical surgical methods for too many important structures lie against the prostate to permit excision of the tumor with a good margin. It differs also in that it grows slowly and is silent until it has spread too